Bandolier 135

Independent evidence-based thinking about health care

On organic manure

Bandolier was bemused by a leaflet dropped through its door advertising 'organic manure'. It wasn't the idea of manure, or organic products, but the pairing of the words. A kindly soul explained that it was probably manure from animals fed on organic products.

So far, so good. But what are the benefits of organic manure, given that Bandolier doesn't keep a market garden? Organic vegetables, fruit, meat, or whatever might be fine, even good, though that is another argument. But manure? Are roses grown on organic manure in some way better than those grown on ordinary manure? And how do you test for organic manure?

Difficult, isn't it? Perhaps there is some warm and cuddly marketing edge here, but warm, cuddly, and manure don't quite seem to go together. There's no common sense here.

Where's the common sense gone?

Common sense is a rather important concept, but one often forgotten. For instance, we know that taking medicines is difficult, especially for older people. In the UK right now, rules on parallel imports of medicines means that some folk receive medicines with non-English package inserts. Most of us would struggle with details of, say, Spanish. It gets much, much more difficult when even the alphabet is different, with Greek or Cyrillic packaging.

It is interesting how common comments about difficulties with medicines like this are becoming. Common sense dictates that it will make for problems, and those problems will be expensive. But perhaps it is someone else's budget.

Bandolier this month examines some areas where common sense and evidence need to be looked at together, starting with a look at recent evidence on cognitive therapy.

In this issue

Cognitive therapy for depression

Does talking make medical conditions better? Preconceptions do not prevent us thinking out criteria necessary to test whether talking works. For talking here, read cognitive therapy, and for a condition, depression.

Trials should include active and placebo comparators to demonstrate superiority of talking to pill taking. That ensures sensitivity. One might choose several outcomes, like some form of depression measure, a defined level of improvement, say, plus a higher level of improvement equivalent to being better (or no worse than if your football team lost on Saturday). A long trial would examine what happened when cognitive therapy stopped.

This is what we have in two reports of a complex randomised trial [1, 2]. The reports indicate that cognitive therapy may be better than we have thought.

Trial design (first 16 weeks [1])

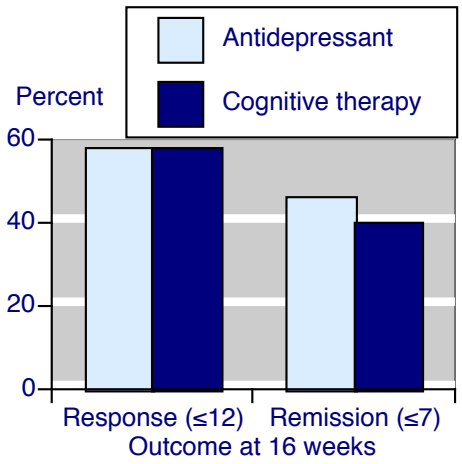
The trial recruited 240 patients who were randomised into three groups, 120 treated with antidepressants, 60 with placebo, and 60 with cognitive therapy. Inclusion criteria were diagnosis of major depressive disorder using standard criteria, and age 18-70 years. All patients had scores of 20 or more on a modified 17-item Hamilton depression rating scale on each of two visits separated by at least a week.

Antidepressant therapy used paroxetine, or identical placebo. The dose was set initially at 10-20 mg a day, and raised in increments based on response and adverse events, to a maximum of 50 mg a day by the sixth week of treatment. Patients had weekly treatment sessions with a psychiatrist for the first four weeks, and every other week thereafter. The duration of treatment with placebo was limited to eight weeks because of ethical considerations, though the whole initial part of the study was conducted over 16 weeks.

While psychiatrists conducted antidepressant therapy, therapists, who were mostly post-doctoral psychologists, conducted cognitive therapy. Guidelines were used with the 50 minute sessions twice weekly for the first four weeks, once or twice weekly for the next eight weeks, and once weekly for the final four weeks.

Outcome was Hamilton depression rating score assessed by a blinded observer. The criterion for response was a score of 12 or less for most of the second eight-week period of treatment. Remission was defined as a score of 7 or less over the same period.

Figure 1: Response and remission at 16 weeks



Results (first 16 weeks)

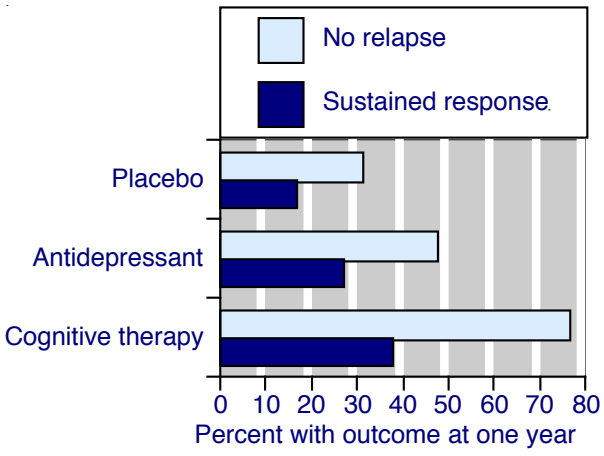
Patients in the trial were mostly (60%) women, with an average age of 40 years. Most (90%) had chronic or recurrent major depressive disorders, had depression for almost 20 years, and about 60% had received previous treatment with antidepressant drugs. The initial mean depression rating score was 23. Trial groups were similar.

Over the whole 16 weeks, 16% of patients treated with antidepressants and 15% of those treated with cognitive therapy withdrew from the trial. These were mainly due to adverse events with antidepressants, and dissatisfaction with treatment with cognitive therapy, and most occurred early. The mean paroxetine dose at the end of 16 weeks was 39 mg daily. The placebo pill group had similar withdrawal rates at eight weeks.

At the end of eight weeks response rates were 50% for antidepressants, 43% for cognitive therapy, and 25% for placebo. Both active treatments were significantly better than placebo, but not each other.

At the end of 16 weeks, 58% of patients in both the antidepressant and the cognitive therapy group had a response. Remission rates were 46% for antidepressant and 40% for cognitive therapy (Figure 1). These were not statistically different from one another.

Figure 2: Relapse and sustained response rates over one year of continuation therapy



Trial design (next year [2])

By 16 weeks 104 patients had responded to treatment. After 16 weeks those responding on antidepressant treatment were re-randomised between continuing antidepressant therapy, or placebo, with the change made over a period during which dose was tapered off, and in a blinded fashion. These patients continued seeing their same psychiatrist, usually every two weeks for the first month and every month thereafter for a year. Patients on cognitive therapy had three booster sessions, at least one month apart.

Outcomes were Hamilton depression rating score assessed by a blinded observer weekly for two weeks, every other week for the next six weeks, and then monthly thereafter. Patients had relapsed if they had a score of 14 or greater on consecutive weeks.

Results (continuation year)

There were 34 patients on ongoing antidepressant therapy, 35 on placebo, and 35 who had had cognitive therapy. Absence of relapse was highest at 76% with cognitive therapy at one year, 47% with antidepressant, and 31% with placebo (Figure 2). Both active treatments were better than placebo. The proportion of patients with a sustained response, defined as completing and responding to acute treatment and staying free from relapse across the one year continuation phase, was better for cognitive therapy and antidepressants than for placebo (Figure 2). Rates were 37%, 27% and 16% respectively.

Comment

These are exciting results from a delightfully designed and conducted study of an explanatory and pragmatic nature. The numbers in the continuation phase were small, and that is one reason why one cannot be over-confident about the results, and why statistical testing and calculating NNTs is probably premature.

The results we have show that cognitive therapy appears to be at least as good in major depression as antidepressants, that the effects are long lasting, and are at least as good as ongoing use of antidepressants.

Some folk might argue about costs, but that is also premature. Much depends on how often people with major depressive disorder are expected to see their psychiatrist, because there were no more visits to the cognitive therapist than to psychiatrist, less over the whole of the study period, and CBT has less drug cost. It makes you think, this. Now we need to try and understand which patient with major depression would do better with which type of therapy.

References:

1 RJ DeRubis et al. Cognitive therapy vs medication in the treatment of moderate to severe depression. Archives of General Psychiatry 2005 62: 409-416.

2 SD Hollon et al. Prevention of relapse following cognitive therapy vs medication in moderate to severe depression. Archives of General Psychiatry 2005 62: 417-422.

Cognitive therapy and panic disorder

We usually test whether interventions work or not in randomised trials. We call this a test of efficacy. Less usual is to see an intervention tested as part of a usual package of care, mimicking its use in a real world situation. This is called a test of effectiveness. Knowing whether an intervention works in practice is much more important than knowing that it works in a trial, so a study demonstrating the value of cognitive behavioural therapy in a real world setting [1] is particularly welcome.

Study

University-affiliated primary care clinics in the western USA formed the setting for the study. Patients were those who were aged 18 to 70 years, fulfilled standard criteria for diagnosis of panic disorder. They had to have at least one panic attack in the previous week, and be willing to accept a combined treatment of anti-anxiety medicine with cognitive behavioural therapy. Exclusions were sensible.

Patients were randomised to usual care or the intervention. Those receiving usual care received whatever their primary care physician thought appropriate, usually pharmacotherapy. The physician knew the results of initial screening and diagnosis, so outcomes could not be attributed to non-recognition of panic disorder. They could be referred or could self-refer to mental health resources thought appropriate.

The intervention used non-physicians (recent masters or doctoral degrees with no cognitive therapy experience) who were trained to deliver evidence-based cognitive therapy targeting panic symptoms, as well as depressive and social anxiety symptoms. Patients received six sessions within the first three months plus six brief telephone contacts. Primary care physicians managed patients' medication, using an algorithm that used a dose titration of SSRI or alternate antidepressant.

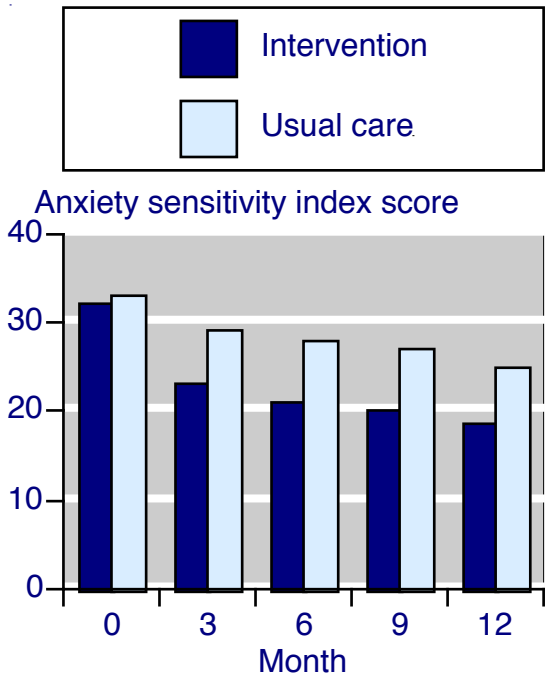
Assessments were made by telephone questionnaire by interviewers blinded to intervention status, at baseline and at three monthly intervals to 12 months. Lots of things were measured, but the main outcomes were remission (no panic attack in last month, minimal anticipation of panic, low agoraphobia score), and response (score of less than 20 on an anxiety sensitivity index).

Results

The 232 patients enrolled had slightly more women than men, with an average age of 41 years. Over 60% had other chronic medical conditions, with social phobia, posttraumatic stress disorder, generalised anxiety and major depression, common psychiatric conditions, in between 30% and 50% of patients. The average panic attack frequency was about 1.5 a week.

By 12 months, remission had occurred in 29% of patients with the intervention, and in 16% of those receiving usual care. The number needed to treat for one more patient receiving the intervention to be in remission at 12 months was 7.4 (95% CI 4.2 to 34).

Figure 1: Anxiety sensitivity scores with cognitive therapy intervention and usual care



Anxiety sensitivity index scores fell in both groups (Figure 1), but significantly more so than those with the intervention. By 12 months, 63% of those with the intervention had a score less than 20, compared with 38% in those receiving usual care. The number needed to treat for one more patient receiving the intervention to have an anxiety score below 20 at 12 months was 4.0 (95% CI 2.7 to 8.0).

At 12 months, depression and disability scores were also significantly lower with intervention than with control. There was no difference in the proportion of patients receiving appropriate anti-panic medication for more than six weeks.

Comment

This is a necessarily complex study excellently reported. No summary can quite do it justice. It may be that the individual contributions of medication and cognitive therapy to the better results with the intervention cannot be discerned, but does that matter?

The point is that the authors have developed a care pathway for treating a common and difficult disorder in primary care, and have shown that it can deliver better results than usual care. Moreover, young graduates with no experience of cognitive therapy delivered the intervention. Clearly this has potential for actual use in primary care by training existing staff.

Reference:
1 PP Roy-Byrne et al. A randomized effectiveness trial of cognitive-behavioural therapy and medication for primary care panic disorder. Archives of General Psychiatry 2005 62: 290-298.

Cost-effectiveness of treatments for major depression in children

Few health economic studies are amenable to simple précis, mainly because they use information from so many different sources, but also because they use different perspectives. They are also often applicable mainly to one health care system, and translate poorly to others. Occasionally one swims into our ken that is really worth a look at. One looking at different treatments for major depression in children [1] is interesting.

Study

The setting for the study was the whole of Australia in 2000, where there were 48,500 new episodes of major depressive disorder in children and adolescents aged six to 17 years. Most (65%) do not consult, and of the 35% who do consult, a third already have an evidence-based treatment. It is those who consult but do not receive evidence-based treatment that formed the cohort for the economic assessment.

The interventions modelled as first-line treatments were 12 one-hour sessions of cognitive behavioural therapy plus two family sessions over 14 weeks, or nine months of treatment with SSRI, three months in the acute phase and six months in a continuation phase, with appropriate clinic visits.

Measurement of health gain was used to calculate disability-adjusted life years. Information on health gain was taken from systematic reviews of cognitive therapy and SSRI in children performed for the study. Costs were taken from Australian standard sources.

Results

The main results are in Table 1. Cognitive therapy was more effective than SSRI, based on limited information. The costs in Table 1 are total costs to the healthcare system if no costs were borne by patients. Incremental cost effectiveness ratios for cognitive therapy and SSRI are for their first line use compared with current practice.

Cognitive therapy using psychologists is cheaper than that using the more expensive psychiatrists, with SSRI intermediate between the two. Using current exchange rates, the values for the ICER are also given as £UK, euro, and $US for easy comparison.

In Australia there is an informal agreement that interventions with costs that fall below $Aus 50,000 per disability adjusted life year saved are probably worthwhile. Iterations used to develop the overall cost fell below this level 100% of the time for cognitive therapy using psychologists, 96% of the time for SSRIs, and 81% of the time for cognitive therapy using psychiatrists.

Comment

What is really interesting about this paper is that it uses the health economic analysis only as the first stage of a process to judge what is best, and what to do. It goes on to use what it calls 'second stage filters' looking at quality of evidence, equity, feasibility and acceptability, and compares these aspects for cognitive therapy versus SSRI.

This takes health economics a fair bit down the road of operational research, and begins better to address issues of overall value, looking at aspects not usually seen in health economic studies. This paper does not just extend the concept that cognitive therapy can be cost effective in a healthcare setting, but it also makes one think outside our usual little box.

References:
1 MM Haby et al. Cost-effectiveness of cognitive behavioural therapy and selective serotonin reuptake inhibitors for major depression in children and adolescents. Australian and New Zealand Journal of Psychiatry 2004 38: 579-591.

Table 1: Major results of cost-effectiveness analysis of cognitive therapy for depression in children and adolescents in Australia, comparing cognitive therapy with SSRI. Costs are cost per disability adjusted life year

Parameter	CBT (psychologist)	CBT (psychiatrist)	SSRI
Efficacy			
Remission with intervention (%)	62	62	46
Remission with control in trials (%)	39	39	30
Imputed NNT	4.3	4.3	6.3
Cost			
Total cost ($Aus, million)	3.7	12	5.4
Incremental CE ratio ($A)	9,000	32,000	23,000
ICER as £UK	3645	12960	9315
ICER as €uro	5220	18560	13340
ICER as $US	6984	24832	17848

Aspartame and headache

Aspartame is a dipeptide sweetener of phenylalanine and aspartic acid. It is widely used in the food industry, especially in diet products to reduce sugar content. Many substances that are sugar free contain aspartame, and individuals who consume large amounts of such products will consume large amounts of aspartame. Since the 1980s when aspartame started to be used, there have been sporadic reports linking it with headache. Bandolier readers asked whether any link had been established, hence this brief review.

Aspartame as a dietary trigger [1]

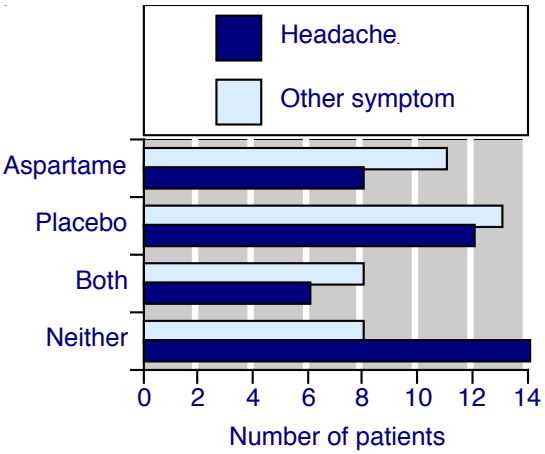
A survey of 190 consecutive patients at a specialist headache unit asked questions about dietary factors and headache. Of the 171 replies, most (77%) were from women, and headache diagnoses were mixed and included migraine, muscle contraction headache, mixed causes, and cluster headaches.

In the sample, 50% reported alcohol as a dietary trigger, 8% aspartame, and 2% carbohydrates. People with migraine more frequently mentioned aspartame (16%) than those with other headache causes.

Randomised aspartame challenge

There have been a number of randomised studies looking at aspartame and biochemistry and adverse events in volunteers, none of which has shown any difference between aspartame and placebo. Typically [2], the studies are well done but small, consisting of a few tens of patients. Though properly randomised and blind, and with a dose of aspartame (15 mg/kg) equivalent to two litres of aspartame sweetened drink, the power of a study with 10 patients is unlikely to uncover a minority of people who were particularly sensitive to aspartame. For comparison purposes, there is about 40 mg aspartame in a packet of sweetener.

Figure 1: Results of single-dose aspartame challenge in aspartame sensitive headache



What is needed is studies in patients who have already declared a sensitivity to aspartame to randomised, blind, challenges of aspartame and placebo under controlled conditions. There are three such trials [3-5], and details of the trial designs and main results are in Table 1.

Although there is some consistency in design and dose of aspartame used, there are a number of possible confounding factors that make interpretation difficult. The main ones are the type of headache and the duration of exposure. It may be that migraine headaches are more likely to be associated with aspartame ingestion, and it might be that longer exposure is more likely to be a trigger.

The problem is that the two longer duration studies have high withdrawal rates, but not obviously more on aspartame than placebo. High withdrawal rates (here only 44 and 56% of patients completed the trials) make interpretation of the results from completers problematical.

In the one trial with no withdrawals [3], meticulously done, there was no acute triggering of headache with aspartame (Figure 1). Neither were any other symptoms more associated with aspartame individually, or collectively.

Table 1: Three main RCTs of aspartame challenge

Parameter	Schiffman [3]	Koehler [4]	Van Den Eeden [5]
Type of patient	History of headache and neurological symptoms associated with aspartame	Migraine not previously associated with aspartame	Headaches after ingesting products containing aspartame
Crossover period	Two one-day challenges with one day washout	2 x 30 days, with one week washout between	4 one week periods, two each of aspartame and placebo
Aspartame dose	30 mg/kg in divided doses between 8 am and noon	1,200 mg/day	30 mg/kg/day
Outcome assessment	Patient and observer during the day		Daily headache diary
Initially randomised	40	25	32
Full completers	40	11	18
Withdrawal	None	?14	12 (equal between aspartame and placebo periods)
Main results	No difference between aspartame or placebo in incidence of headaches or other symptoms. No difference in headache intensity, onset time, or duration	Mean of 3.6 headaches on aspartame, 1.5 on placebo	33% of days with headache on aspartame, 24% on placebo. More pronounced difference in those very sure that headaches were associated with aspartame. No difference in intensity or duration of headache

Comment

The answer seems to be that there is no completely satisfactory answer. On the basis of what we have, it is probably fair to say that if aspartame is a triggering factor for headache, it probably affects migraine, rather than other forms of headache. In addition, it is unlikely that it precipitates acute attacks, but perhaps prolonged exposure might cause more frequent headaches.

The lesson is probably to consider aspartame a trigger in some people with migraine who consume lots of diet drinks or other diet products. For those with a limited exposure to aspartame, it is unlikely to be a problem.

Postscript

For those people who do have aspartame-triggered migraines, some treatments can be a bit problematical. Two such patients had migraines shown by exclusion diets to be associated with aspartame [6]. Their migraines were well controlled with standard therapies including triptans, but a wafer melt formulation of one triptan consistently made headaches worse, not better. It turns out that these melt formulations contain 4 mg aspartame – about a tenth of that in a packet of sweetener. An example of the importance of case reports in contributing important information.

References:
1 RB Lipton et al. Aspartame as a dietary trigger of headache. Headache 1988 29: 90-92.
2 KA Lapierre et al. The neuropsychiatric effects of aspartame in normal volunteers. Journal of Clinical Pharmacology 1990 30: 454-460.
3 SS Schiffman et al. Aspartame and susceptibility to headache. New England Journal of Medicine 1987 317: 1181-1185.
4 SM Koehler, A Garos. The effect of aspartame on migraine headache. Headache 1988 28: 10-13.
5 SK Van Den Eeden et al. Aspartame ingestion and headaches: a randomized crossover trial. Neurology 1994 44: 1787-1793.
6 LC Newman, RB Lipton. Migraine MLT-down: an unusual presentation of migraine in patients with aspartame-triggered headaches. Headache 2001 41: 899-901.

Compensation status and surgical outcome

The history of worker compensation, or other compensation, and medical outcomes is a difficult and tortuous one, which Bandolier has no hope of reviewing. For those with an interest in its history, though, there is at least one good reference [1].

What about outcome after surgery and compensation status? A new meta-analysis suggests that poor outcomes may be twice as likely in compensated versus non-compensated individuals [2].

Systematic review

The study sought published papers of any trial of surgical intervention in which compensation status was reported, and compared results according to that status. A compensated patient was defined as one who received workers' compensation payments for their condition, or who experienced litigation as a result of their preoperative condition. The minimum size was set at a single compensated and a single non-compensated patient.

Any surgery was included, but not rehabilitation, injections, or similar interventions. Region-specific outcome scores were the main outcome of interest, but generalised function scores, health outcome scores like SF-36, patient satisfaction score, or a pain score were also used. Satisfactory or unsatisfactory outcomes were as reported in the publications, with general descriptions like fair, poor or failure included in unsatisfactory.

Results

The search identified 211 studies, of which 175 described a worse outcome in the compensation group, 30 described no difference, and one described better outcomes in the compensation group. Five did not comment.

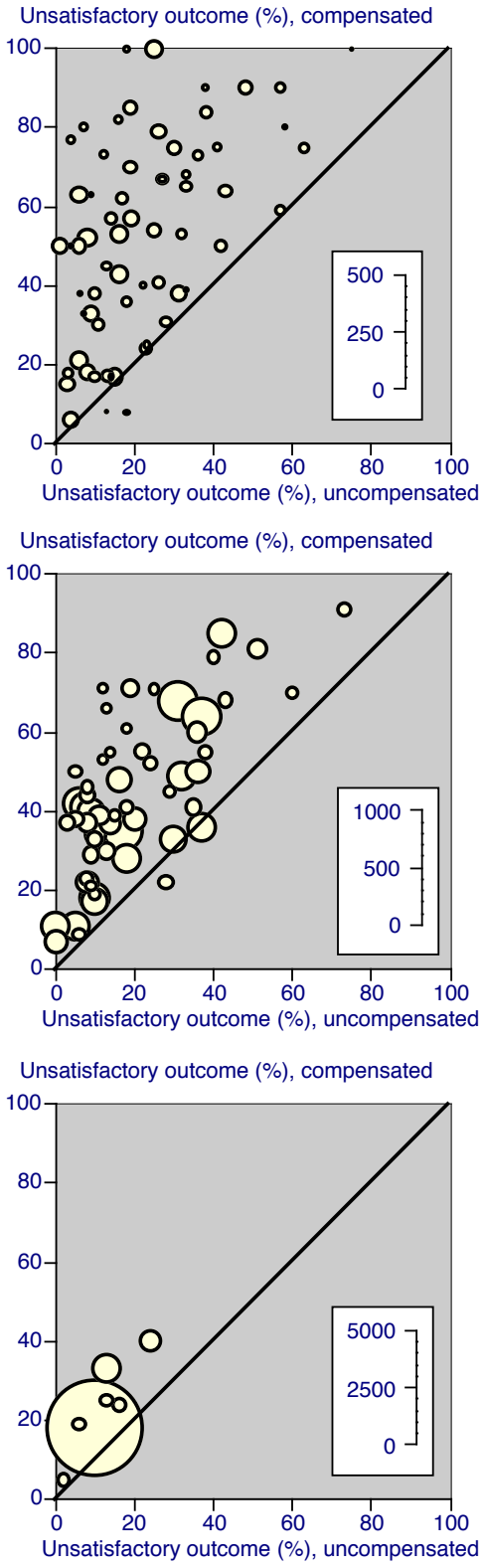
Dichotomous scores were available in 129 studies with over 20,000 patients, ranging in size from nine to 4,200 patients. The median size was 74 patients, and all but seven of the studies had fewer than 500 patients. The results differed somewhat depending on the size of the study (Table 1, Figures 1-3).

The smallest studies, those below the median size, had the highest proportion (51%) of unsatisfactory outcomes with surgery (Figure 1). The NNT in this group of patients was 3.3 (3.0 to 3.7).

Table 1: Results analysed according to size of study

	Number of		Percent unsatisfactory outcome			
Size of study	Trials	Patients	Compensated	Noncompensated	Relative risk (95% CI)	NNT (95% CI)
Below median (≤74)	65	2809	51	21	2.4 (2.2 to 2.7)	3.3 (3.0 to 3.7)
Moderate (77-499)	57	9245	45	19	2.1 (2.0 to 2.2)	3.8 (3.5 to 4.1)
Largest (≥500)	7	8427	22	12	2.0 (1.8 to 2.2)	10 (8.8 to 13)
All studies	**129**	**20481**	**37**	**16**	**2.1 (2.0 to 2.2)**	**4.8 (4.5 to 5.1)**

Figures 1-3: Unsatisfactory surgical outcome in smallest, larger, and largest trials



Larger studies between 75 and 499 patients in size had a lower, but still high, proportion (45%) of unsatisfactory outcomes with surgery (Figure 2). The NNT in this group of patients was higher at 3.8 (3.5 to 4.1).

The seven largest studies with more than 500 patients in each had the lowest proportion (22%) of unsatisfactory outcomes with surgery (Figure 3). The NNT in this group of patients was much higher at 10 (9 to 13).

Other sensitivity analyses had limited value because of the propensity of smaller studies to have bigger effects, especially when there were so many small studies. But study design, follow up time, type of procedure, or type of compensation seemed to make little difference to the overall conclusion.

Comment

A number of lessons are to be learned here. First is that of size. We forget at our peril that small studies tend to overestimate effects, and the smallest allowable trial here was of two (2) patients. Some trials had only two or three patients in one of the groups. In this example only 14% of all patients were in half of all trials (the smallest), but 41% were in the largest seven trials.

Both large and small studies reported a similar direction of result, the magnitude of which was larger in the smallest trials of below median size. The magnitude of the difference declined with increasing size. So the large difference in small trials (1 more unsatisfactory outcome for every 3 compensated versus non-compensated patients) became less important in the largest trials (1 more unsatisfactory outcome for every 10 compensated versus non-compensated patients).

We know from other circumstances that small studies often lack the rigour of large studies, which is why we see a bias towards greater effects in small studies. The implication is that we should disregard them in favour of larger studies. But how large is large enough? As we have no quality filter for the studies in the review, this leaves us in a bit of a pickle. We cannot rule out that the difference between compensated and non-compensated is due to bias from poor study quality.

The largest trials demonstrated only half the differential effect of compensation status compared with the whole sample of trials. Moreover, as none of the trials was randomised by compensation status, we do not know whether patients who were being compensated had the same degree of severity as those who were not being compensated. So while we do not know it to be the case, we cannot rule out that the compensated were initially worse than non-compensated, which is why there is a difference.

All in all, a bit of analysis takes what is on the face of it a straightforward result that fits our prejudices nicely, and challenges whether there is any effect at all. But that probably takes it too far, and concerns about bias and baseline differences are not justified. The best we can say is that it is likely that unsatisfactory results from surgery are more common in people who are being compensated, but that we have no good idea just how much more common.

References:

1 G Mendelson. Compensation and chronic pain. Pain 1992 48: 121-123.
2 I Harris et al. Association between compensation status and outcome after surgery. JAMA 2005 293: 1644-1652.

Pharmacist case management of type 2 diabetes

Most chronic diseases have some patients who do not do well with usual care. Reasons will be different for different people, but what to do remains problematical. One strategy might be to provide extra, individualised education, help, and feedback for a period. A randomised trial [1] indicated that directed input from a clinical pharmacist can improve results for patients with poorly controlled type 2 diabetes.

Study

The setting was a primary care university-affiliated clinic with 10 primary care physicians and an established clinical pharmacist as part of the team. Patients were those with type 2 diabetes whose recent Hb_{A1c} value was 8% or more, who were younger than 70 years and who did not have serious co-morbid conditions. Randomisation was balanced across four strata of Hb_{A1c} (8-8.9%, 9-9.9%, 10-10.9%, and ≥11%).

The intervention was by a clinical pharmacist. It consisted of a one hour educational and medicines management visit, with emphasis on self-care, medications, and screening processes for complications. Subsequent visits were as needed, with monthly telephone contact. Periodic reviews provided status updates to physicians. Non-intervention patients received usual care.

The main outcome was Hb_{A1c} at the end of follow up over 12 to 24 months. Other assessments were take up of screening and examinations.

Results

Eighty patients were randomised. Their average age was 51 years, and the average baseline Hb_{A1c} was 10.2%. There were no differences in medications used between intervention and control patients.

The mean decrease in Hb_{A1c} in intervention periods over an average 14 months follow up was 2.1%. For control patients over an average 15 months it was 0.9%. The result was statistically significant, with and without any imputed values from the few patients lost to follow up.

Figure 1: Decrease of HbA1c (%) for intervention over control according to initial HbA1c value

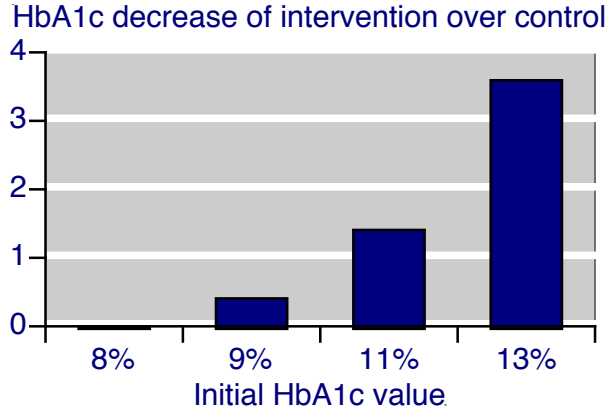


Table 1: Recent processes and examinations (shaded significantly different)

Process	Percent with measure	
	Control	Intervention
HbA1c	83	92
LDL	86	100
Retinal examination	74	97
Urine albumin screen	86	95
Foot examination	63	92

Intervention was much more effective in those with the highest (worse) Hb_{A1c} levels. Figure 1 shows that the additional decrease over control patients receiving usual care was 3.6% for those with average baseline Hb_{A1c} of 13%, and 1.4% for those with a baseline of 11%. In addition, there were significantly increased rates of cholesterol measurement, retinal examination, and foot examination in intervention patients (Table 1).

Comment

This may not be rocket science, but it does demonstrate that relatively simple interventions for the patients who need help can make a big difference, however good usual care may be. The setting was real world, and the intervention simple. This was an intervention that could be introduced for many primary care practices, and with the potential for extrapolation to other chronic diseases. Key to success may well have been the way physicians and pharmacist acted as a team, and how the pharmacist made the patient a de-facto member of that team.

Because resources, especially staff time, are limited, being able to determine which patients are most likely to respond to an intervention is obviously important. In this case it was those with an initial Hb_{A1c} of about 10% or more. Here the results were particularly good, with an absolute reduction of 3-6% in Hb_{A1c} in those with the worst glycaemic control. This would be expected to produce significant and substantial reductions in risk of microvascular complications. The UKPDS indicated that a 1% reduction in HbA1c levels leads to a 21% reduction in the risk of diabetes related complications and death.

Reference:
1 HM Choe et al. Proactive case management of high risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. American Journal of Managed Care 2005 11: 253-260.